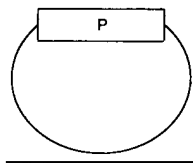


AMENDMENTS TO THE CLAIMS

The present amendment amends claims 8, 11, 12, 18, 19, 32 and 33, and adds claims 44-52. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the following claims are in the case:

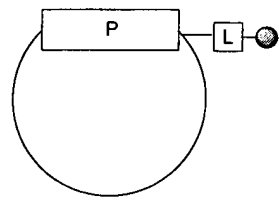
Claims 1-7 cancelled

8. (Currently Amended) ~~A method according to claim 1,~~ A method of synthesis of a cyclic peptide or peptidomimetic compound of General Formula I




General Formula I

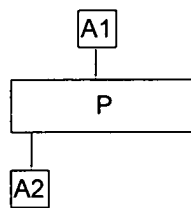
or General Formula II



General Formula II

where L is a linker unit, linking the cyclic peptide to a solid support  in which the cycle is a monocycle, bicycle or higher order cycle comprising 1 to 15 monomers, which is carried out in solution, comprising the steps of:

- a) Preparing a linear peptide of General Formula III



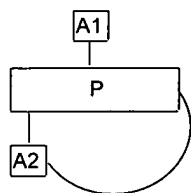
General Formula III

where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

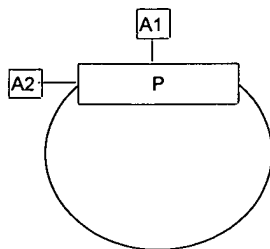
A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

b) Activating the C-terminus to form a cyclic peptide of General Formula IV:



General Formula IV

- c) Permitting the peptide of General Formula IV to rearrange via a ring contraction reaction (~~which may occur spontaneously~~) to form a cyclic peptide of General Formula V; and optionally



General Formula V

- d) Subjecting the cyclic peptide of General Formula V to a deprotection reaction to remove the groups A1 and A2 to yield the desired cyclic peptide of General Formula I.
9. (Original) A method according to claim 8, in which P is a linear peptide of 1 to 10 monomers.
10. (Original) A method according to claim 9, in which P is a linear peptide of 1 to 5 monomers.

11. (Currently Amended) A method according to claim 8, in which A1 ~~and/or A2~~ is left attached to the peptide, A2 is left attached to the peptide or both A1 and A2 are left attached to the peptide.

12. (Currently Amended) A method according to claim 11, in which A1 ~~and/or A2~~ is subsequently linked to a solid support, derivatised, or linked to another cyclic peptide or peptidomimetic compound; A2 is subsequently linked to a solid support, derivatised, or linked to another cyclic peptide or peptidomimetic compound; or both A1 and A2 are subsequently linked to a solid support, derivatised, or linked to another cyclic peptide or peptidomimetic compound.

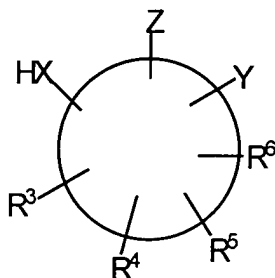
13. (Previously Presented) A method according to claim 8, in which A1 is a reversible N-substituent.

14. (Original) A method according to claim 13, in which A1 is a 2-hydroxy-4-methoxybenzyl, 2-hydroxybenzyl or 2-hydroxy-6-nitrobenzyl substituent.

15. (Previously Presented) A method according to claim 8, in which A2 is eliminated by spontaneous ring contraction.

16. (Previously Presented) A method according to claim 8, in which A2 comprises a nucleophile that reacts rapidly with a C-terminus to form an initial large ring, which then contracts either spontaneously, or upon heating or additional chemical treatment.

17. (Original) A method according to claim 16, in which A2 is thiol or hydroxyl.
18. (Currently Amended) A method according to claim 8, in which A2 is an irreversible substituent, A2 is removed after ring contraction, or A2 is eliminated spontaneously upon ring contraction.
19. (Currently Amended) A method according to claim 8, in which A2 is a compound of general formula (a):



(a)

in which the ring

- (a) optionally comprises one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulphur;
- (b) is of ~~5 to 7~~ 6 atoms;
- (c) comprises 3 carbon atoms substituted respectively by XH, Z, and Y; and
- (d) is additionally substituted by ~~groups R³ and R⁴ when the compound is a 5-membered ring, or is additionally substituted by groups R³, R⁴, and R⁵ when the~~

~~compound is a 6-membered ring, or is additionally substituted by groups R³, R⁴, R⁵ and R⁶ when the compound is a 7-membered ring,~~

in which

X is oxygen, sulphur, CH₂O-, or CH₂S-;

Y is an electron-withdrawing group;

Z is any group which allows the formation of a covalent carbon-nitrogen bond; and

R³, R⁴ and R⁵ are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, alkoxy, aryloxy,

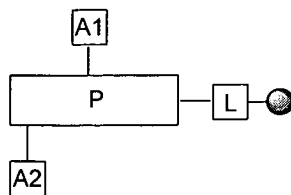
XH or Y, or a covalent linkage to a solid support, and

in which R³ and R⁴ or R⁴ and R⁵ can optionally together with the ring form a 5-, 6-, or 7-membered ring.

Claims 20-31 cancelled

32. (Currently Amended) A method of solid phase synthesis of a cyclic peptide, comprising the steps of

a) synthesis of a linear solid support-bound peptide of General Formula XIII,



General Formula XIII

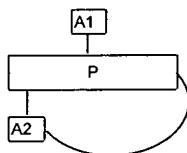
where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

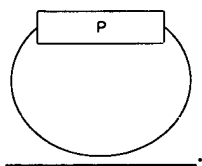
L is a linker between any atom of the peptide and the solid support, and

- b) subjecting the peptide of General Formula XIII to cyclisation and concomitant cleavage from the solid support to yield a cyclic peptide of General Formula XIV,



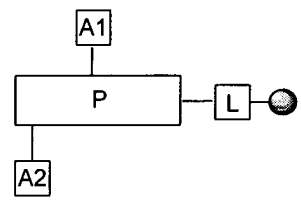
General Formula XIV

- c) subjecting the cyclic peptide of General Formula XIV to ring contraction (~~which may be spontaneous~~), and
- d) if A1 is a reversible substituent, cleaving the groups A1 and A2 to yield the desired cyclic peptide of General Formula I;



33. (Currently Amended) A method of solid phase synthesis of a cyclic peptide, comprising the steps of;

- a) synthesis of a linear solid support-bound peptide of General Formula XIII,



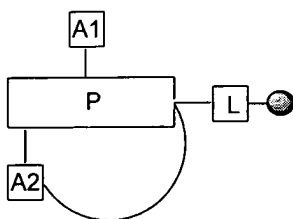
where P is a linear peptide of 1 to 15 monomers;

A1 is one or more N-substituents, either reversible or non-reversible, on the peptide backbone, or is a chemical moiety that forces a *cis* conformation of the backbone, and

A2 is a covalently-bonded group of atoms comprising a reactive functionality to form an initial large cyclic peptide prior to ring contraction to the desired substituted cyclic peptide;

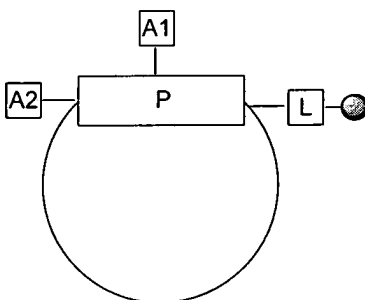
L is a linker between any atom of the peptide and the solid support, and

- b) subjecting the linear peptide to cyclisation on the solid support to yield a cyclic peptide of General Formula XV,



General Formula XV

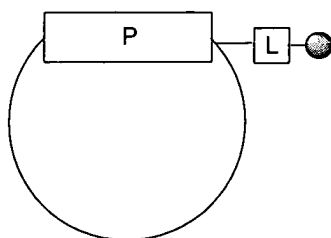
- c) subjecting the cyclic peptide to ring contraction (~~which may occur spontaneously~~) to yield a cyclic peptide of General Formula XVI,



General Formula XVI

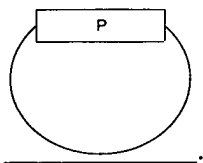
and either

- d) cleaving groups A1 and A2 while the peptide is bound to the solid support to yield a resin-bound cyclic peptide of General Formula II, or



General Formula II

- e) subjecting the cyclic peptide to deprotection and concomitant cleavage from the solid support to yield the desired cyclic peptide of General Formula I;



34. (Original) A method according to claim 33, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed separately.
35. (Original) A method according to claim 33, in which side chain deprotection of the peptide, removal of A1 and cleavage from the solid support are performed concurrently.

Claims 36-38 cancelled

39. (Previously Presented) A method according to claim 32, in which one or more of the monomers carries a side chain protecting group.

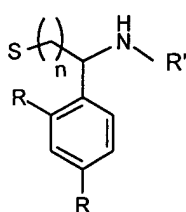
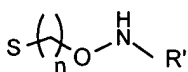
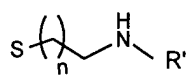
40. (Previously Presented) A method according to claim 33, in which one or more of the monomers carries a side chain protecting group.

Claims 41-43 cancelled

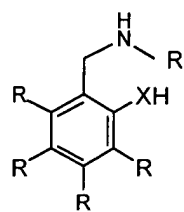
44. (New) A method according to claim 8, in which A1 is a cis-amide bond surrogate.

45. (New) A method according to claim 44, in which the cis-amide bond surrogate is a tetrazole.

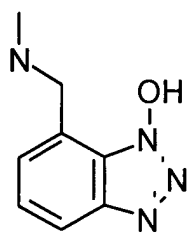
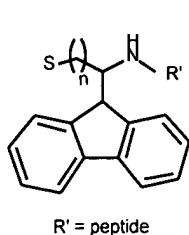
46. (New) A method according to claim 8, in which A2 is selected from the group consisting of



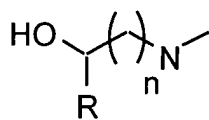
R=H,OMe



R=H,NO₂
X=O,S



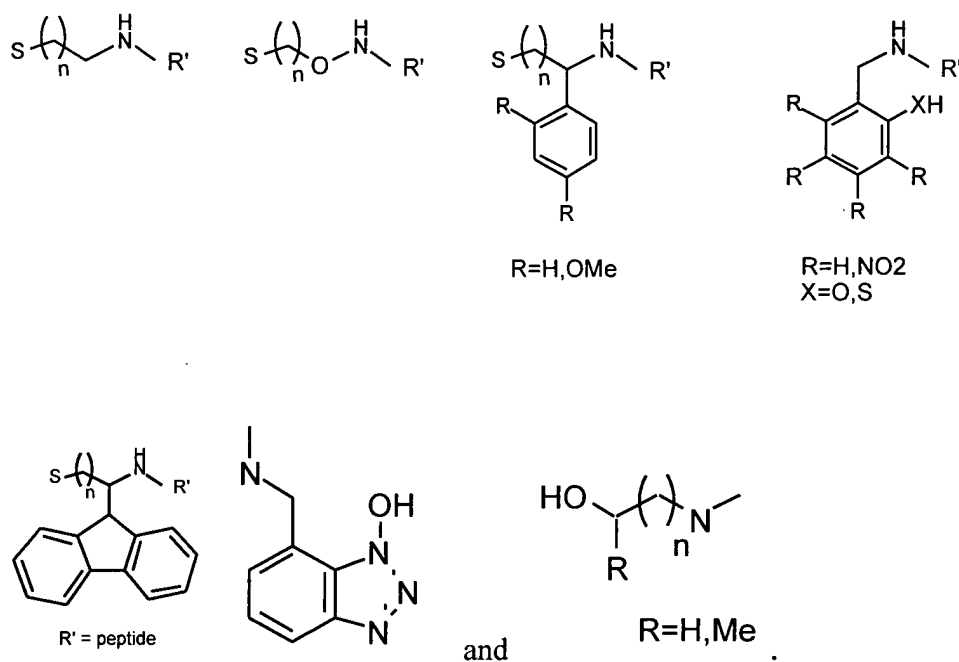
and



R=H,Me

47. (New) A method according to claim 8, in which A2 is 6-nitro-2-hydroxybenzyl, 4-nitro-2-hydroxybenzyl or 5-nitro-2-hydroxybenzyl.

48. (New) A method according to claim 19, in which A2 is selected from the group consisting of



49. (New) A method according to claim 19, in which A2 is 6-nitro-2-hydroxybenzyl, 4-nitro-2-hydroxybenzyl or 5-nitro-2-hydroxybenzyl.

50. (New) A method according to claim 8, in which the ring contraction reaction occurs spontaneously.

51. (New) A method according to claim 32, in which the ring contraction reaction occurs spontaneously.

52. (New) A method according to claim 33, in which the ring contraction reaction occurs spontaneously.